# <Division of Multidisciplinary Chemistry> Supramolecular Biology

# Division of Multidisciplinary Chemistry
## - Supramolecular Biology -

http://www.scl.kyoto-u.ac.jp/~umeda/index.htm

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## Scope of Research

We have undertaken the molecular biology, cell biology and behavioral genetics approaches to study the role of biological membrane systems in controlling animal morphogenesis and behavior. The membrane is a complex supramolecular complex formed by a noncovalent self-assembly of proteins, lipids, and carbohydrates. Our long term objective is to understand the fundamental principles underlying the dynamism of complex membrane systems and to provide a clue to reconstruct an artificial supramolecular membrane complex. Current research topics are as follows:

(1) Identification of a series of proteins that regulate molecular motion of lipid molecules and elucidation of their role in cellular and animal morphogenesis.

(2) Establishment of a series of *Drosophila* mutants with aberrant temperature preference (*atsugari, samugari*, etc) and elucidation of the molecular relationship between the temperature-responding membrane systems and animal behaviors.

## Research Activities (Year 2005)

### Presentations

Lipid Field in Biological Membranes. Umeda M. JST Workshop. 23 - 24 March, Hamamatsu.

Mass Spectrometry of Phospholipids Using an Intense Femtosecond Laser. Kato U., Shimizu S., Taniuchi K., Sakabe S., Umeda M. The 47th Japanese Conference on the Biochemistry of Lipids, 2 - 3 Jun, Kanazawa.

A New Approach for Molecular Lipid Biology Using Drosophila. Umeda M. Japanese Drosophila Research Conference. 7 - 9 July, Awaji.

Membrane Lipids and Cell Size Control. Umeda M., Taniuchi K., Inadome H., Shishioh N., Kato U. The 78th Annual Meeting of The Japanese Biochemical Society. 19 - 22 October, Kobe.

Regulation of Actin Filament Assembly by Dynamic Redistribution of Plasma Membrane Phosphatidy Lethanolamine. Inadome H., Emoto K., Umeda M. The 78th Annual Meeting of the Japanese Biochemical Society. 19 - 22 October, Kobe.

Generation of the Hypomorphic Allele of Stearoyl-CoA Desaturase in *Drosophila*. Takahara K., Takeuchi K., Yamamoto D., Umeda M. The 78th Annual Meeting of the Japanese Biochemical Society. 19 - 22 October, Kobe.

Membrane Lipid Dynamics and Cellular Morphogenesis. Umeda M., Taniuchi K., Inadome H., Shishioh N., Kato U. The 43rd Annual Meeting of The Biophysical Society of Japan. 23 - 25 November, Sapporo.

### Grants

Umeda M, Cellular Morphogenesis Based on the Positional Information of Membrane Phospholipids. Grant-in-Aid for Scientific Research (A)(2), 1 April 2003 - 31 March 2007.

Umeda M, Identification of Genes Involved in Thermo-

## Regulation of Membrane Phospholipid Dynamics and Its Role in Cell Morphogenesis

Biological membranes consist of a phospholipid bilayer where phospholipid molecules move not only laterally but also across the two layers of the bilayer membranes. Although it is generally believed that the organized movements of membrane phospholipids play a pivotal role in regulating the structure of biomembranes, the molecular mechanisms underlying the controlled movements of membrane phospholipids are still poorly understood. To identify the molecules that regulate the movements of membrane phospholipids, we have isolated a series of yeast mutants with disordered organization of membrane phospholipids. By analyzing the genes defective in these mutants, we have identified a novel membrane protein, Ros3p, which is required for the translocation of phospholipids across the yeast plasma membrane. Ros3p is highly conserved among various organisms including worm, fly and mammals, implicating a general role for cellular functions. To reveal the biological functions of ROS3 family proteins, we have established a series of mutant flies in which the expression level of ROS3 protein is genetically manipulated. We found that the reduced expression of ROS3 protein caused marked reduction in the size of cells during larval development (Figure.1a). Overproduction of ROS3 protein resulted in increased cell size and disorganized organ structure (Figure.1b). These results suggest that ROS3 family proteins play a role in controlling the size and morphology of cells through regulating the movement of membrane phospholipids.

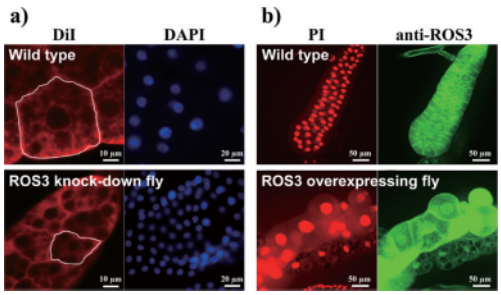


**Figure 1.** Changes in the expression of ROS3 proteins caused abnormal cell size and organ structure during larval development of *Drosophila*.
a) Fat body cells in the wild type and the ROS3 knock-down flies were stained with a lipophilic dye (DiI) and a nucleic marker (DAPI). Each cell was framed in a white line.
b) Salivary gland cells in the wild type and the ROS3 overexpressing flies were stained with anti-ROS3 antibody and a nucleic marker (PI).

## The Molecular Mechanisms of Thermoregulation in Animals: The Role of Dystroglycan in Determination of the Thermoregulatory Set Point in Drosophila

Temperature is a critical variable with a profound impact on living organisms. A wide variety of animals sense the environmental temperature, move toward to thermally comfortable zone, and tend to remain for relatively long periods. The tendency to remain still in this preferred range may be regarded as a mechanism to keep the animals within a range of temperatures, namely the thermoregulatory set point, which is optimal for most physiological metabolic processes. Moreover the preferred temperature differs among species as well as among individuals within a species. Progress has been made in the identification of molecules involved in the sensation of peripheral temperature, but the molecular mechanisms that determine the thermoregulatory set point remain poorly understood. In an effort to identify genes involved in temperature preference, we searched for mutations that affect temperature preference of *Drosophila melanogaster*, and identified the *atsugari* mutant, which shows a preference for unusually low temperature. We showed that the *atsugari* phenotype was caused by the reduced expression of dystroglycan. We also found that the *atsugari* mutant exhibited a striking tolerance to cold temperature (Figure2). These results suggest that the defective expression of dystroglycan in the *atsugari* mutant results in downward resetting of the thermoregulatory set point as well as the lower limit of cold tolerance. Although dystroglycan has been characterized as a central molecule involved in the pathogenesis of muscular dystrophy, our studies revealed a novel role for dystroglycan in thermoregulatory functions of animals.

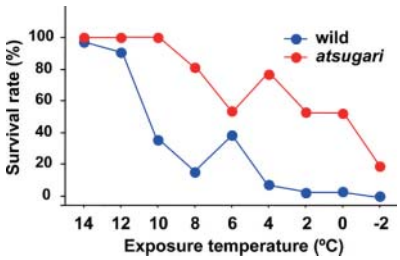


**Figure 2.** The *atsugari* mutant showed a striking tolerance to cold temperatures. Third-instar larvae of the *atsugari* mutant and wild type were exposed to cold temperatures under constant darkness for 24 h. After exposure, they were placed at 25°C for 48 h and checked for survival.

regulatory Behavior of Insects. Special Cooperation Funds for Promoting Science and Technology from the MEXT Agency of Japan. 1 April 2002 - 31 March 2006.

Takeuchi K, Development of a New *Drosophila* Model for Studying Muscular Dystrophy. Grant-in-Aid for Exploratory Research, 1 April 2004 - 31 March 2007.

Inadome H, Analysis of the Asymmetric Distribution of the Phospholipids in the Golgi Apparatus in Yeast. Grant-in-Aid for Scientific Research for Young Scientists (B), 1 April 2005 - 31 March 2007.